

Phytotherapy with *Hordeum Vulgare*: A Randomized Controlled Trial on Infants with Jaundice

GHOLAMREZA PANAHADEH¹, ABOLFAZL KHOSHDEL², MORTEZA SEDEHI³, AZAM ALIAKBARI⁴

ABSTRACT

Introduction: Jaundice is one of the most common causes of admission to hospital in newborns which is often associated with several complications.

Aim: The present study was conducted to evaluate the effect of *H. vulgare* in reducing jaundice.

Materials and Methods: In this double-blind, randomized controlled trials 70 term infants hospitalized due to jaundice in 2014 were enrolled. Control group was treated with full-time phototherapy alone using LED except when the infants were breastfed and case group with phototherapy, as per the protocol in the control group, along with and topical *H. vulgare* seed flour

three times a day. Data were analysed using and analysis of covariance (ANCOVA) and paired t-test in SPSS version 16.0.

Results: There was a significant difference in mean indirect bilirubin level between the two groups $p < 0.05$, such that the mean indirect bilirubin level was higher in the control group. Furthermore, no significant difference was seen in direct bilirubin level between the two groups at discharge $p > 0.05$.

Conclusion: *H. vulgare* flour can cause decrease in indirect bilirubin. Because the rate of decrease in indirect bilirubin can be effective in preventing severe complications due to bilirubinemia, *H. vulgare* can be used as a complementary therapy to treat jaundice.

Keywords: *Hordeum vulgare* flour, Neonatal jaundice, Phototherapy

INTRODUCTION

Jaundice is a disease of early days of life due to accumulation of bilirubin under the skin, mucus membranes, and sclera. Jaundice can be caused by incompatibility between the blood of mother and foetus, haematoma dissolution, bruising of the baby's body, infection, liver diseases, and hematologic diseases, such as G6PD deficiency [1,2], and unknown causes [3]. Jaundice or indirect hyperbilirubinemia is one of the prevalent diseases among infants in Iran [3] and other regions worldwide. It has been reported that approximately 60% of term infants and 80% of preterm infants acquire jaundice in the first week of life [1]. This disease is the cause of 75% of infants' hospitalizations [4], and imposes stupendous costs on health care system [5]. Jaundice is a complicated disorder due to hyperbilirubinemia. When unconjugated bilirubinemia begins to increase, it may cause neurotoxicity and brain damage in infants [6] such that chronic jaundice can lead to a dangerous complication called bilirubin encephalopathy or kernicterus. Kernicterus can cause neurological disorders, auditory nerve damage, choreoathetoid, cerebral palsy, and other problems [7].

Phototherapy is considered a common and leading treatment for jaundice since long time. Despite having certain advantages and being considered to be significant around the world, it may cause a number of short-term complications such as disruption in maternal-infant emotional interaction, disturbance of thermal equilibrium, dehydration, electrolyte imbalance, "bronze baby" syndrome, disturbance of infant circadian rhythm, decrease in the duration of exclusive breastfeeding, and DNA damage [8,9].

It is therefore necessary to search for new therapies. Currently, medicinal plants are considered a good source for preparation of new drugs, not only for jaundice but also for other diseases [10-14]. Complementary medicine plays a significant role, accompanied with modern medicine, such that in addition to phototherapy, several herbal drugs are used to treat jaundice in Iran [15]. Barley (*Hordeum vulgare* L.) is an herbaceous plant from family Poaceae. *H. vulgare* is used to treat several diseases, including jaundice, in Iranian traditional medicine [16].

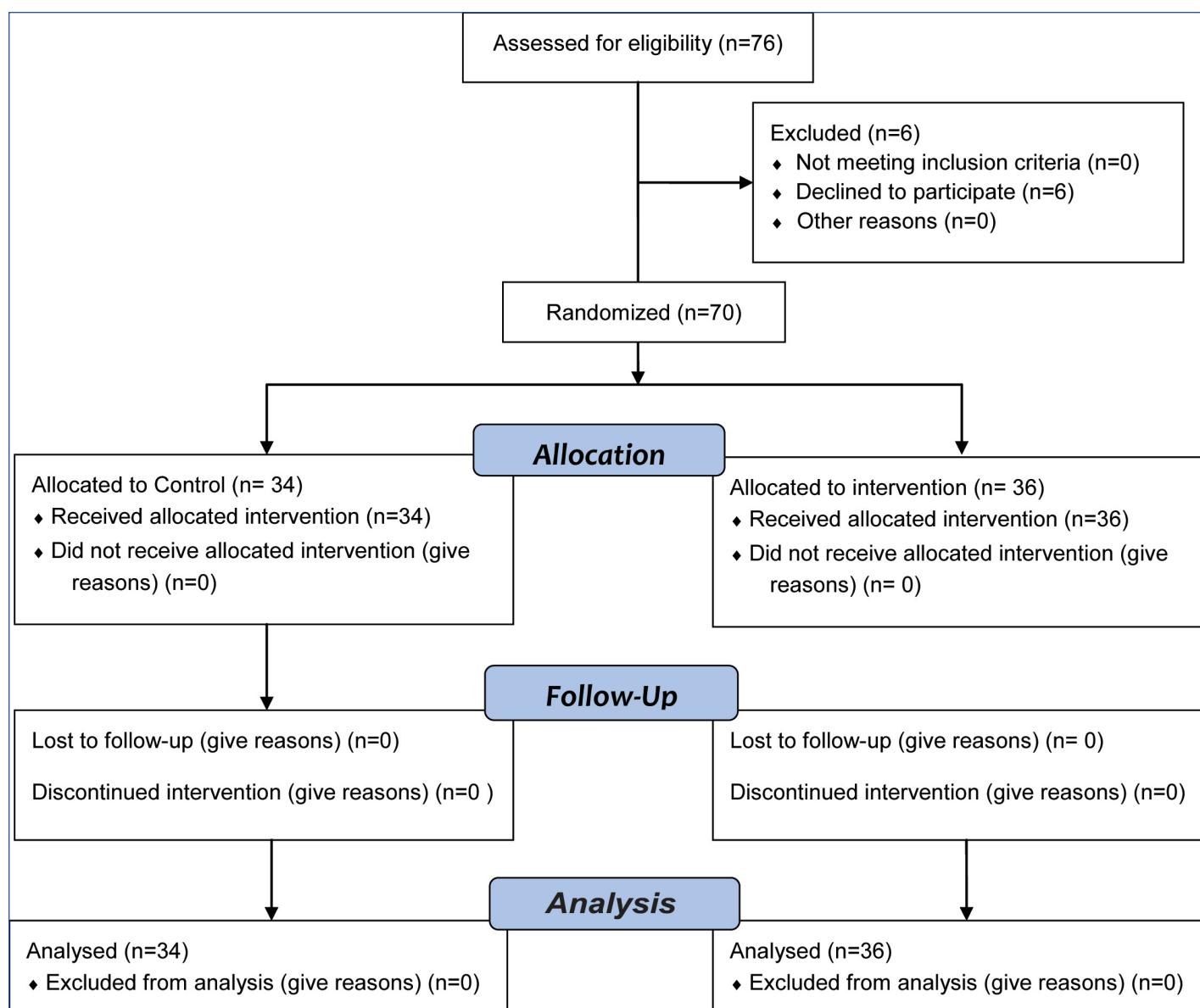
Use of traditional medicinal plants can be a simple and accessible approach to treat neonatal jaundice with few side effects. Because *H. vulgare* flour is widely used as an effective phytotherapy according to ethnobotanical studies, this study was conducted to investigate the effect of *H. vulgare* flour on jaundice.

MATERIALS AND METHODS

In this double-blind, randomized controlled trial, 70 term infants hospitalized due to jaundice in the neonatal care unit of Hajar Hospital of Shahrekord, Southwest Iran in July-December, 2014 were enrolled [Table/Fig-1]. The inclusion criteria were: being term, healthy, and over three-day-old, having total serum bilirubin level in between 12 mg/dl to 18 mg/dl, weighing 2500-4000 gm, breastfeeding, no increase in direct bilirubin by over 2 mg/dl, and no risky symptoms such as lethargy, lack of breastfeeding, fever, blood incompatibility of mother and baby, polycythemia, anaemia, and family history of severe jaundice.

The presence of clinical and laboratory infection, dehydration, G6PD, incompatibility of blood types (ABO), positive Coombs test, direct bilirubin levels of over 2 mg/dl, total bilirubin of over 18 mg/dl and allergic reaction to *H. vulgare* flour were considered exclusion criteria. The infants were randomly and alternately divided into two groups (n: 34 and 36) by random number table. At the beginning of the study, all parents provided informed consent to their infants' participation in the study. Breastfeeding continued when the infants stayed in the hospital. The protocol of this study was approved by the Research Committee of the Shahrekord University of Medical Sciences (the approval code: 91-10-25).

Once every 24 hours, the blood samples were taken to assess bilirubinemia levels. The infants in the control group received full-time phototherapy alone using LED except when the infants were breastfed and the case group did phototherapy, per the protocol in the control group, and topical *H. vulgare* seed flour three times a day. *H. vulgare* flour (150 g) was sieved and then applied on the whole body of the infants in the case group except head, face, and around umbilical cord. Then, the flour was rinsed and phototherapy started.



[Table/Fig-1]: Consort flow diagram of the study.

Afterwards, complete blood count, the mothers and the infants blood type, reticulocyte count, Coombs test, G6PD, and total, direct, and indirect bilirubinemia were examined. At baseline, the two groups were matched for hospital stay, birth weight, direct and indirect bilirubin level. The required samples were taken and sent to laboratory.

STATISTICAL ANALYSIS

After a sufficient number of infants were enrolled and the data were gathered, analysis of covariance (ANCOVA) and paired t-test in SPSS 16.0 were used to compare the data of the two groups.

RESULTS

Overall, 70 infants (36 cases and 34 controls) were studied. A total of 21 (30%) infants had blood type A, nine (8.12%) blood type B, 38 (54.2%) blood type O, and two (2.8%) blood type AB. Sixty five (92.8%) infants were found as Rh positive and the rest Rh negative. Regarding birth order, 35 (50%) infants were the first child of the family and the rest second-ninth child. Only one (1.42%) infant was the ninth child of the family.

At baseline, direct and indirect bilirubin levels of the two groups were compared and were not found to be significantly different ($p>0.05$). The duration of hospital stay was apparently in the two groups. There was no significant difference in weight, baseline direct bilirubin, and baseline indirect bilirubin between the cases and the controls [Table/Fig-2].

According to ANCOVA, there was a significant difference in mean indirect bilirubin level between the two groups at discharge ($p<0.05$), such that the mean indirect bilirubin level was higher in the control group. No significant difference was seen in direct bilirubin level between the two groups at discharge ($p>0.05$) [Table/Fig-3].

Variable	Groups	Mean (standard deviation)	p-value
Hospital stay (Day)	Phototherapy + <i>H. vulgare</i> flour	3.16±1.04	0.34
	Phototherapy	2.91±1.18	
Weight (gm)	Phototherapy + <i>H. vulgare</i> flour	3.03±0.45	0.22
	Phototherapy	3.17±4.88	
Baseline indirect bilirubin	Phototherapy + <i>H. vulgare</i> flour	14.55 2.52	0.13
	Phototherapy	15.30 1.57	
Baseline direct bilirubin	Phototherapy + <i>H. vulgare</i> flour	0.42±0.17	0.27
	Phototherapy	0.46±0.17	

[Table/Fig-2]: Comparison of hospital stay, weight, and bilirubin level between the two groups at baseline.

Variable	Groups	Mean±SD	p-value
Indirect bilirubin at discharge	Phototherapy + <i>H. vulgare</i> flour	9.92±1.37	0.009
	Phototherapy	10.71±1.13	
Direct bilirubin at discharge	Phototherapy + <i>H. vulgare</i> flour	0.58±0.17	0.51
	Phototherapy	0.55±0.15	

[Table/Fig-3]: Comparison of direct and indirect bilirubin levels between the two groups at discharge.

DISCUSSION

This study was conducted to investigate the effect of *H. vulgare* flour in decreasing jaundice. According to Iranian traditional medicine, *H. vulgare* is used to serve several purposes, including jaundice treatment, in many regions of Iran [15,16].

Phytochemical and phytotherapeutic investigations have indicated that *H. vulgare* contains fibrous, water-soluble compounds such as β -glucans which can exert hypocholesterolemic effects and contribute to the regulation of glycaemia. *H. vulgare* has various properties, including antilactagogue, anti-inflammatory, antioxidant, diuretic, aphrodisiac, antiprotozoal, antiviral, demulcent, astringent, febrifuge, digestive, expectorant, hypocholesterolemic, antimutagenic, refrigerant, sedative, stomachic, tonic properties, and emollient. It can be used as a compress to treat wound, as well [17]. Presumably, antioxidants absorbed by the skin, can enhance liver function and improve hepatocytes activity, that facilitate the process of converting indirect bilirubin to the conjugated bilirubin.

H. vulgare can induce antioxidant effects because of having phenolic compounds and certain compounds such as tocopherol, catechin, and lutein. The ethanolic and methanolic compounds in *H. vulgare* can serve as metal chelating agents [18,19]. This plant can be used as a food to enhance liver function and serve as a hepatoprotective agent [20]. Since vitamins A, E, and D are absorbed through skin epithelial liposomes [21], the carrying role of active compounds of *H. vulgare* flour can be considered for phospholipid-containing liposomes in skin epithelial cells.

Jaundice is associated with increase in oxidative stress. Laboratory studies have demonstrated that use of some *H. vulgare* species can help oxidative stress markers decrease and antioxidant markers increase in rats. As a result, *H. vulgare* stops adverse histological and biochemical changes in the liver [22] and is useful to regulate liver enzymes [20].

The significance of *H. vulgare* antioxidant properties is because of the fact that oxidative stress in infants with jaundice leads to decrease in certain antioxidants such as glutathione and ascorbic acid. This condition is exacerbated after phototherapy, which can intensify neurological damage in infants [23]. Besides that, the improvement of liver function is an important issue which should be considered to treat jaundice.

The phenolic components of *H. vulgare* are relatively high and have antioxidant activities [24-27]. Antioxidants can be effective in treating some other disorders [28-33]. Therefore, *H. vulgare*, which contains high level of antioxidant activity, may be effective in these conditions, too.

Unconjugated or indirect hyperbilirubinemia in the first or second week of life can be due to increased production of bilirubin and liver inability to excrete bilirubin [23]. During phototherapy, bilirubin absorbs optical energy and the bilirubin existing in skin is converted, by several photochemical reactions, to certain products that can be excreted through kidneys and bile [23].

A limitation of the present study is that the effective compounds of *H. vulgare* flour were not extracted. Moreover, the action mechanisms of this flour were not investigated. Future studies are recommended to investigate the effects of oral consumption of *H. vulgare*-based purified products on jaundice or the preventive effects of these compounds before delivery in newborns at risk.

CONCLUSION

H. vulgare flour can cause decrease in indirect bilirubin and has no contribution to reducing direct bilirubin and duration of hospital stay. As it is important to treat jaundice rapidly and prevent severe associated complications, *H. vulgare* can be used as a complementary therapy to treat jaundice.

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PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Paediatrics, Shahrekord University of Medical Sciences, Shahrekord, Chaharmahal va Bakhtiari, Iran.
2. Associate Professor, Department of Paediatrics, Shahrekord University of Medical Sciences, Shahrekord, Chaharmahal va Bakhtiari, Iran.
3. Assistant Professor, Department of Epidemiology and Biostatistics, Shahrekord University of Medical Sciences, Shahrekord, Chaharmahal va Bakhtiari, Iran.
4. General Practitioner, Department of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Chaharmahal va Bakhtiari, Iran.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Gholamreza Panahandeh,
 Assistant Professor, Department of Paediatrics, Shahrekord University of Medical Sciences,
 Shahrekord, Chaharmahal va Bakhtiari, Iran.
 E-mail: gholamrezapanahandeh@gmail.com

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